UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Date: April 23, 2002

MEMORANDUM

SUBJECT: LINDANE: REVISION OF EXPOSURE ASSESSMENT FOR COMMERCIAL SEED TREATMENT PLANT WORKER

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TO: Rebecca Daiss
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THRU Susan Hummel, Senior Scientist
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Please find attached the occupational exposure assessment for lindane:

DP BARCODE: D282419

Pesticide Chemical Code: 009001

EPA MRID Nos: 45200002

PHED: No

1.0 INTRODUCTION

In March 2001 HED provided an exposure/risk assessment for seed treatment use of lindane (1). The document included on farm treatments (using wheat as the typical treatment), planting the treated seed, and commercial seed treatment facilities. The assessment indicated that the study used for commercial seed treatment was of poor quality and probably did not address changes in the technology that have occurred since the study was conducted. Since that time a study measuring exposures of workers treating canola seed with HELIX 289S (a mixture of thimethozam, difenconazole, metalaxyl, and fludioxonil). The study was reviewed jointly by EPA and PMRA (MRID 45200002) (2). The HELIX 289S Study is comprehensive occupational exposure study designed and conducted to quantify potential exposure to thiamethoxam, formulated as a flowable liquid, during commercial treatment of canola seed. Lindane end-use products for canola use are liquids (flowable formulation). Lindane products for grower use on small grains, corn, and sorghum are wettable powders. In the absence of more formulation specific data, HED believes the HELIX Study provides the best data available for assessing exposure/risk from commercial seed treatment with lindane. HED has reevaluated the estimates of exposure and risk from treatment of wheat and canola seed with lindane using unit dermal and inhalation exposures provided in the HELIX 289FS Study.

2.0 EXPOSURE ASSESSMENT

2.1 Summary of Toxicity Endpoints

Toxicity endpoints used for the revised occupational exposure assessment are the same as those used for the previous assessment. They are summarized below and in Table 1.

Dermal

The critical study selected for short- and intermediate-term dermal risk assessment was the Developmental Neurotoxicity Study in rats. A 90-day dermal toxicity study in rabbits was available; the NOAEL was 10 mg/kg/day and the LOAEL was 60 mg/kg/day based on hepatic toxicity. The HIARC did not consider this study to be appropriate for risk assessment and instead selected an oral endpoint due to: 1) the concern for developmental effects as seen in pups in the developmental neurotoxicity study, 2) developmental effects are not evaluated in the dermal toxicity study, 3) the dermal toxicity study was conducted in the rabbit, while the increased susceptibility was seen in rat pups via an oral route, and 4) this endpoint will be protective of dermally exposed workers. For developmental toxicity, the NOAEL was 1.2 mg/kg/day and the LOAEL was 5.6 mg/kg/day based on reduced pup survival, decreased body weights and body weight gains during lactation, increased motor activity, and decreased motor activity habituation. The target MOE is 100 (10X for interspecies variation and 10X for intraspecies variation) for occupational exposure. Since an oral endpoint was selected, a 10% dermal absorption factor will be used for route to route extrapolation.

Inhalation

The critical study for inhalation risk assessment for lindane is an 90-Day Inhalation Toxicity. Lindane was administered by inhalation to groups of 12 male and 12 female Wistar rats at nominal concentrations of 0, 0.02, 0.10, 0.50, or 5.0 mg/m^3, 6 h/day for 90 days. Lindane was detected in the brain, liver, fat, and serum of all exposed rats. The HIARC established a NOAEL of 0.5 mg/m^3 for this risk assessment based on clinical signs (diarrhea and piloerection) seen at day 14 after exposure and continuing for 20 days at the highest concentration tested (5 mg/m^3). This NOAEL is applicable and appropriate only for short-term exposure risk assessment because the effects were seen during this period of exposure. For intermediate exposures, the NOAEL is 0.5 mg/m^3 (0.13 mg/kg) based on increased kidney weights and bone marrow effects. For inhalation risk assessments for occupational exposure, the target MOE is 100 (10X for intraspecies variation and 10X for interspecies variation). Long-term inhalation exposure is not expected.

Table 1. Doses and Toxicological Endpoints Selected for Risk Assessment of Lindane

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY TYPE/ MRID
Acute Dietary- general population	NOAEL= 6 mg/kg UF = 100	LOAEL is 20 mg/kg based on increased grip strength, increased motor activity	Acute Neurotoxicity in Rats/ 44769201
Acute RfD = 0.06 mg/kg/day		**aPAD = 0.02 mg/kg/day**	
Chronic Dietary	NOAEL= 0.47 mg/kg/day UF = 300	LOAEL is 100 ppm (4.81 mg/kg/day) periacinar hepatocyte hypertrophy, increased liver/spleen weight, decreased platelets	Chronic Feeding and Carcinogenicity in Rats 41094101, 41853701 42891201
Chronic RfD = 0.0047 mg/kg/day		**cPAD = 0.0016 mg/kg/day**	
Short-Term [1] (Dermal)	NOAEL= 1.2 mg/kg/day	LOAEL is 50 ppm based on reduced pup survival, decreased body weights and body weight gains during lactation, increased motor activity, and decreased motor activity habituation.	Developmental Neurotoxicity Study in Rats (oral) 45073501
Intermediate-Term [1] (Dermal)	NOAEL= 1.2 mg/kg/day	LOAEL is 50 ppm based on reduced pup survival, decreased body weights and body weight gains during lactation, increased motor activity, and decreased motor activity habituation.	Oral Developmental Neurotoxicity Study in Rats (oral) 45073501
Long-Term [1] (Dermal)	NOAEL= 0.47 mg/kg/day	LOAEL is 100 ppm (4.81 mg/kg/day) periacinar hepatocyte hypertrophy, increased liver/spleen weight, decreased platelets	Chronic Feeding and Carcinogenicity in Rats 41094101, 41853701 42891201
Dermal Absorption Factor = 10%			

Table 1. Doses and Toxicological Endpoints Selected for Risk Assessment of Lindane			
EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY TYPE/ MRID
Short Term [1] (Inhalation)	0.13 mg/kg/day (0.5 mg/m^3)	NOAEL is based on clinical signs (diarrhea, piloerection) seen at day 14 and continuing for 20 days	90-Day Inhalation Toxicity / 00255003
Intermediate Term [1] (Inhalation)	0.13 mg/kg/day (0.5 mg/m^3)	LOAEL is 5.0 mg/m^3 based on increased kidney weights of female rats and bone marrow effects.	90-Day Inhalation Toxicity / 00255003
Long Term [2] (Inhalation)	N/A	N/A	N/A

[1] An MOE of 100 was selected

[2] Exposure thru this route for this duration is not expected

2.2 Revised Exposure and Risk Estimates

HED has reevaluated the estimates of exposure and risk from treatment of wheat and canola seed with lindane using median unit dermal and inhalation exposures provided in the HELIX 289FS Study. Unit exposures used for this assessment are summarized in Table 2. Unit exposure data from the HELIX study are presented in detail in Appendix A.

Table 2. Unit Dermal and Inhalation Exposures of Workers During Seed Treatment and Handling of Treated Seed[1]	
Median Unit Dermal and Inhalation Exposures	
Treater - Closed Transfer - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves	
Dermal (n=17)	0.83 µg/lb/ai
Inhalation (n=17)	0.12 µg/lb/ai
Cleaner - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves	
Dermal (n=7)	6.70 µg/kg bw
Inhalation (n=7)	1.20 µg/kg bw
Bagger/Sewer/Stacker - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves	
Dermal - chemical resistant coveralls (n=34)	0.26 µg/lb/ai
Dermal - Cotton/polyester coveralls (n=19)	0.30 µg/lb/ai
Inhalation (n=53)	0.06 µg/lb/ai
Forklift Operator - cotton/polyester coveralls over long-sleeve shirt, long pants; chemical resistant gloves	
Dermal (n=12)	0.08 µg/lb/ai
Inhalation (n=12)	0.008 µg/lb/ai

[1] Commercial Seed Treatment Plant Worker Exposure Study with Helix 289FS Seed Treatment on Canola (MRID 452000-02)

The application rate in the HELIX study was 400 gm thiamethoxam/100 kg seed (0.88 lb/220000 lb seed). The throughput of seed of 7000 kg/hr (15400 lb/hr), 6800 kg /hr(14960 lb/hr), 5000 kg/hr (11000 lb/hr), 5000 kg/hr (11000 lb/hr), 10000 kg/hr (22000 lb/hr) for sites 1 to 5, respectively. The following assumptions were used to estimate exposure:

1) The throughput of seed for both wheat and canola is 22000 lb/per hour or 176000 lbs per 8 hour day.

2) The application rate for wheat is 0.043 lb ai per hundred weight of seed. The application rate for canola is 1.5 lb (high-end) and 0.75 lb (low-end) ai per hundredweight of seed.

3) Pounds handled per day for wheat:

   lbs handled per day wheat = 176000 lbs/day x 0.043 ÷ 100 lbs = 76 lbs/day
   lbs handled per day canola (high-end) = 176000 lbs/day x 1.5 ÷ 100 lbs = 2640 lbs/day
   lbs handled per day canola (low-end) = 176000 lbs/day x 0.75 ÷ 100 lbs = 1320 lbs/day

4) Median unit dermal and inhalation exposures were used based on data distribution.

5) Worker body weight for dermal exposure = 60 kg (female body weight used for developmental endpoint)

6) Worker body weight for inhalation exposure = 70 kg

7) The short term and intermediate term dermal NOAEL is 1.2 mg/kg/day (10% dermal absorption factor is required for route to route extrapolation)
   The short and intermediate term inhalation NOAEL is 0.13 mg/kg/day.

   The resulting daily exposures and MOEs are provided in the Table 3.

Table 3 - Daily Exposures, Short Term and Intermediate MOEs for Commercial Seed Treatment Plant Worker Exposure

Exposure Scenario (Scenario #)	Application Rates (lb ai/100 lbs seed or Lb/A)	Amount Handled per Day (lbs a.i.)	Unit Exposure (mg/lb ai)[a]		Daily Exposure (mg/kg/day)		Short-Term MOEs & Intermediate Term MOES	
			Dermal	Inhalation	Dermal[b]	Inhalation[s]	Dermal[c]	Inhalation[e]
Treater - Closed Transfer - chemical resistant coveralls over long-sleeved shirt, longpants, chemical resistant gloves (1)	1.5 (canola high-end)	2640	0.00083	0.00012	0.036	0.0045	330	29
	0.75 (canola low-end)	1320	0.00083	0.00012	0.018	0.0023	660	57
	0.043 (wheat)	76	0.00083	0.00012	0.0010	0.00013	11000	1000
Bagger/Sewer /Stacker - chemical resistant coveralls over long-sleeved shirt, longpants, chemical resistant gloves - (2)	1.5 (canola high-end)	2640	0.00026	0.00006	0.011	0.0023	1000	57
	0.75 (canola low-end)	1320	0.00026	0.00006	0.0057	0.0011	2100	120
	0.043 (wheat)	76	0.00026	0.00006	0.00033	6.48E-05	37000	2000
Bagger/Sewer /Stacker cotton/polyester coveralls over long-sleeved shirt, longpants, chemical resistant gloves (3)	1.5 (canola high-end)	2640	0.0003	0.00006	0.013	0.0023	910	57
	0.75 (canola low-end)	1320	0.0003	0.00006	0.0066	0.0011	1800	120
	0.043 (wheat)	76	0.0003	0.00006	0.00038	6.5E-05	32000	2000
Forklift Operator - chemical resistant coveralls over long-sleeved shirt, longpants, chemical resistant gloves (4)	1.5 (canola high-end)	2640	0.00008	8E-06	0.0035	0.00029	34000	450
	0.75 (canola low-end)	1320	0.00008	8E-06	0.0018	0.00015	6800	900
	0.043 (wheat)	76	0.00008	8E-06	0.00010	8.3E-06	119000	16000
Cleaner - chemical resistant coveralls over long-sleeved shirt, longpants, chemical resistant gloves (5)	1.5 (canola high-end)	NA	NA	NA	0.0067	0.0012	1800	110
	0.75 (canola low-end)	NA	NA	NA	0.0067	0.0012	1800	110
	0.043 (wheat)	NA	NA	NA	0.0067	0.0012	1800	110

a Median unit dermal and inhalation unit exposures

b Daily Dermal Exposure (mg/kg/day) = unit exposure (mg/lb ai) x amount handled per day (lbs a.i.) / bw (60 kg).

c Dermal MOE = Oral NOAEL (1.2 mg/kg) / [daily exposure (mg/kg/day) x dermal absorption factor (10%)].

d Daily Inhalation Exposure (mg/kg/day) = inhalation unit exposure (mg/lb ai) x amount handled per day (lbs a.i.) / body weight (70 kg). Cleaner daily inhalation exposures, measured in mg/kg/day, were taken directly from the HELIX study.

e Inhalation MOE = NOAEL (0.13 mg/kg/day) / daily exposure (mg/kg/day).

3.0 Conclusions

For the five commercial seed treatment plant worker scenarios assessed, two scenarios resulted in MOEs of concern (MOE <100). The inhalation MOEs are of concern for canola seed treatment for both the treater and bagger/sewer/stacker scenarios. All other scenarios result in MOEs that are not of concern.

REFERENCES

1) Memorandum from D. Jaquith (RRB4) to S. Shallal (RRB4) titled "OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND RECOMMENDATIONS FOR THE RE REGISTRATION ELIGIBILITY DECISION DOCUMENT FOR LINDANE", dated March 16, 2001.

2) Memorandum from Steven Weiss to Donna Davis titled "STUDY REVIEW: COMMERCIAL SEED TREATMENT PLANT WORKER EXPOSURE STUDY WITH HELIX 289FS SEED TREATMENT ON CANOLA", dated March 22, 3001.

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APPENDIX A

The HELIX 289S Study is comprehensive occupational exposure study designed and conducted to quantify potential exposure to thiamethoxam, formulated as a flowable liquid, during commercial treatment of canola seed. Lindane end-use products for canola use are liquids (Flowable formulation). Lindane products for grower use on small grains, corn, and sorghum are wettable powders. In the absence of more formulation specific data, HED believes the HELIX Study provides the best data available for assessing exposure/risk from commercial seed treatment with lindane.

The full field phase monitored 89 full day replicates across 5 representative commercial seed treatment sites and 4 representative job categories. Statistical descriptors of unit dermal and inhalation exposures (µg/kg handled for all job categories except for cleaners which are provided in µg/kg bw) are provided in Table 1.

Table 1. Unit Dermal and Inhalation Exposures of Workers During Seed Treatment and Handling of Treated Seed[1]

Unit Dermal and Inhalation Exposures							
Subpopulation and Route	Range		Central Tendency			90th Percentile	Standard Deviation
	Min	Max	AM	GM	Median		
Treater - Closed Transfer - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves µg/kg ai (ug/lb/ai)[2]							
Dermal (n=17)	0.54 (0.25)[2]	73.20 (33.3)	7.36 (3.35)	2.39 (1.09)	1.83 (0.83)	13.17 (5.99)	17.48 (7.95)
Inhalation (n=17)	0.06 (0.027)	0.53 (0.24)	0.27 (0.12)	0.24 (0.11)	0.26 (0.12)	0.38 (0.17)	0.12 (0.055)
Cleaner - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves (µg/kg bw)							
Dermal (n=7)	2.77	81.98	19.37	9.21	6.69	46.06	28.57
Inhalation (n=7)	0.31	3.30	1.54	1.15	1.19	3.19	1.19
Bagger/Sewer/Stacker - Chemical-Resistant coveralls over long-sleeve shirt, long pants; chemical resistant gloves µg/kg ai (ug/lb/ai)[2]							
Dermal - chemical resistant coveralls (n=34)	0.084 (0.038)	5.88 (2.67)	0.90 (0.41)	0.61 (0.28)	0.58 (0.26)	1.63 (0.74)	1.02 (0.46)
Dermal - Cotton/polyester coveralls (n=19)	0.07 (0.032)	3.86 (1.75)	1.29 (0.59)	0.81 (0.37)	0.67 (0.30)	3.18 (1.45)	1.23 (0.56)
Inhalation (n=53)	0.008 (0.0036)	1.26 (0.57)	0.25 (0.11)	0.14 (0.06)	0.14 (0.06)	0.65 (0.30)	0.29 (0.13)
Forklift Operator - cotton/polyester coveralls over long-sleeve shirt, long pants; chemical resistant gloves µg/kg ai (ug/lb/ai)[2]							
Dermal (n=12)	0.09 (0.041)	4.20 (1.91)	0.72 (0.33)	0.32 (0.15)	0.18 (0.08)	1.29 (0.59)	1.18 (0.54)
Inhalation (n=12)	0.003 (0.0014)	1.001 (0.46)	0.105 (0.048)	0.022 (0.010)	0.017 (0.0077)	0.064 (0.029)	0.283 (0.129)

[1] Commercial Seed Treatment Plant Worker Exposure Study with Helix 289FS Seed Treatment on Canola (MRID 452000-02)
[2] Numbers in parentheses have been converted to µg per lb ai